

Claims

1. A method for preventing or treating a glutamate excitotoxicity-associated neurological disorder in a subject, comprising:

administering to a subject in need of such treatment and otherwise free of indications
5 for treatment with an antimicrobial compound, an effective amount of the antimicrobial compound to treat the neurological disorder.

2. The method of claim 1, wherein the antimicrobial compound is cloxyquin or an analog, derivative, or variant thereof that increases glutamate transport activity.

10 3. The method of claim 1, wherein the antimicrobial compound is citrinin or an analog, derivative, or variant thereof that increases glutamate transport activity.

15 4. The method of claim 1, wherein the antimicrobial compound is iodoquinol or an analog, derivative, or variant thereof that increases glutamate transport activity.

5. The method of claim 1, wherein the antimicrobial compound is oxyquinoline or an analog, derivative, or variant thereof that increases glutamate transport activity.

20 6. The method of any of claims 1-5, wherein the glutamate excitotoxicity-associated neurological disorder is selected from the group consisting of cerebrovascular accident, stroke, seizure, head and spinal cord trauma, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, epilepsy, glaucoma, and hepatic encephalopathy.

25 7. The method of any of claims 1-5, wherein the subject is human.

8. The method of any of claims 1-5, wherein the compound is linked to a targeting molecule.

30 9. The method of claim 8, wherein the targeting molecule's target is a cell selected from the group consisting of glial cells and neuronal cells.

10. The method of any of claims 1-5, wherein the compound is a pro-drug.

11. The method of any of claims 1-5, wherein the compound is administered prophylactically to a subject at risk of having a glutamate excitotoxicity-associated neurological disorder.

12. The method of any of claims 1-5, wherein the mode of administration is selected from the group consisting of: implantation, mucosal, injection, inhalation, and oral.

13. The method of any of claims 1-5, wherein the compound is administered in combination with an additional drug for treating a neurological disorder.

14. The method of any of claims 1-5 further comprising administering a compound selected from the group consisting of nordihydroguaiaretic acid, ebselen, flunisolid, hydrocortisone, and analogs, derivatives, and variants thereof, for prevention and/or treatment of a neurological disorder.

15. A method for treating a subject having a condition characterized by glutamate excitotoxicity comprising

administering to a subject in need of such treatment a cloxyquin, citrinin, iodoquinol, or oxyquinoline compound, in an amount effective to increase glutamate transport activity, wherein the subject is free of symptoms otherwise calling for treatment with the cloxyquin, citrinin, iodoquinol, and oxyquinoline.

16. The method of claim 15, wherein the condition characterized by glutamate excitotoxicity is selected from the group consisting of cerebrovascular accident, stroke, seizure, head and spinal cord trauma, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, epilepsy, glaucoma, and hepatic encephalopathy.

17. The method of claim 15, wherein the subject is human.

18. The method of claim 15, wherein the cloxyquin, citrinin, iodoquinol, or oxyquinoline compound is linked to a targeting molecule.

19. The method of claim 18, wherein the targeting molecule's target is a cell selected from the group consisting of glial cells and neuronal cells.

5 20. The method of claim 15, wherein the compound is a pro-drug.

21. The method of claim 15, wherein the compound is administered prophylactically to a subject at risk of having the condition characterized by glutamate excitotoxicity.

10 22. The method of claim 15, wherein the mode of administration is selected from the group consisting of: implantation, mucosal, injection, inhalation, and oral.

23. The method of claim 15, wherein the compound is administered in combination with an additional drug for treating a neurological disorder.

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24. The method of claim 15 further comprising administering a compound selected from the group consisting of nordihydroguaiaretic acid, ebselen, flunisolide, hydrocortisone, and analogs, derivatives, and variants thereof.

20 25. A method of evaluating the effect of candidate pharmacological agents on glutamate transport activity, comprising:

contacting a test cell sample with a candidate pharmacological agent;

contacting the test cell sample with glutamate,

determining the effect of the candidate pharmacological agent on the activity of

25 glutamate transport in the test cell sample relative to the activity of glutamate transport in a control cell sample contacted with glutamate and not contacted with the candidate pharmacological agent, wherein a relative increase or relative decrease in the activity of glutamate transport in the test cell sample indicates modulation of glutamate transport activity by the candidate pharmacological agent.

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26. The method of claim 25, wherein the test cell sample comprises embryonic mouse spinal cord motor neuron hybrid cells (MN-1).

27. The method of claim 25, wherein the glutamate is detectably labeled.

28. The method of claim 25, wherein the amount of glutamate transport activity is determined by measuring the amount of detectably labeled glutamate taken up by the test cell sample.

29. The method of claim 25, wherein a relative increase in the activity of glutamate transport in the test cell sample indicates the modulator is a glutamate transport enhancing agent.

30. The method of claim 25, wherein a relative decrease in the activity of glutamate transport in the test cell sample indicates the modulator is a glutamate transport inhibitory agent.

31. A method for preparing an animal model of a disorder characterized by glutamate excitotoxicity, comprising introducing a glutamate transport inhibitory agent into a non-human animal.

32. The method of claim 31, further comprising detecting in the non-human animal symptoms of a disorder characterized by glutamate excitotoxicity.

33. The method of claim 31, wherein the animal model is a model for a neurological disorder.

34. The method of claim 33, wherein the disorder selected from the group consisting of: cerebrovascular accident, stroke, seizure, head and spinal cord trauma, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, epilepsy, glaucoma, and hepatic encephalopathy.

35. A kit comprising a package housing
a first container containing an antimicrobial compound, and
instructions for using the antimicrobial compound in the prevention and/or treatment
of a neurological disorder.

36. The kit of claim 35, wherein the antimicrobial compound is selected from the group consisting of: cloxyquin, citrinin, iodoquinol, oxyquinoline, and analogs, derivatives, and variants thereof.

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37. The kit of claim 35, further comprising a second container containing a medication and instruction for the using the compounds and medication for prevention and/or treatment of a neurological disorder.

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38. The kit of claim 35, further comprising a container containing a compound selected from the group consisting of nordihydroguaiaretic acid, ebselen, flunisolide, hydrocortisone, and analogs, derivatives, and variants thereof; and instructions for using the compounds for prevention and/or treatment of a neurological disorder.

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39. The kit of claim 35, wherein the antimicrobial compound is formulated for delivery to neuronal cells.

40. The kit of claim 35, wherein the antimicrobial compound is formulated for delivery to glial cells.

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41. The kit of claim 35, wherein the antimicrobial compound is formulated for sustained release.

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42. A method of modulating glutamate transport activity in a subject in need of such treatment, comprising administering a compound selected from the group consisting of nordihydroguaiaretic acid (NDGA), ebselen, flunisolide, hydrocortisone, and analogs, derivatives, and variants thereof, in an amount effective for modulating glutamate transport activity.

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43. The method of claim 42, wherein the subject is human.

44. The method of claims 42, wherein the compound is linked to a targeting molecule.

45. The method of claim 44, wherein the targeting molecule's target is a cell selected from the group consisting of glial cells and neuronal cells.

46. The method of claim 42, wherein the compound is a pro-drug.

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47. The method of claims 42, wherein the compound is administered prophylactically to a subject at risk of having a glutamate excitotoxicity-associated neurological disorder.

48. The method of claim 47, wherein the glutamate excitotoxicity-associated neurological disorder is selected from the group consisting of cerebrovascular accident, stroke, seizure, head and spinal cord trauma, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, epilepsy, glaucoma, and hepatic encephalopathy.

49. The method of claim 42, wherein the mode of administration is selected from the group consisting of: implantation, mucosal, injection, inhalation, and oral.

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50. The method of claim 42, wherein the compound is administered in combination with an additional drug for treating a neurological disorder.

51. The method of claim 42, wherein modulating glutamate transport activity is increasing glutamate transport activity.

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52. A method of decreasing glutamate excitotoxicity in a subject in need of such treatment, comprising administering a compound selected from the group consisting of nordihydroguaiaretic acid (NDGA), ebselen, flunisolide, hydrocortisone and analogs, derivatives, and variants thereof, an amount effective for decreasing glutamate excitotoxicity in the subject.

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53. The method of claim 52, wherein the glutamate excitotoxicity is associated with a neurological disorder selected from the group consisting of cerebrovascular accident, stroke, seizure, head and spinal cord trauma, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, epilepsy, glaucoma, and hepatic encephalopathy.

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54. The method of claim 52, wherein the subject is human.

55. The method of claim 52, wherein the compound is linked to a targeting molecule.

5 56. The method of claim 55, wherein the targeting molecule's target is a cell selected from the group consisting of glial cells and neuronal cells.

57. The method of claim 52, wherein the compound is a pro-drug.

10 58. The method of claim 52, wherein the compound is administered prophylactically to a subject at risk of having a glutamate excitotoxicity-associated neurological disorder.

59. The method of claim 52, wherein the mode of administration is selected from the group consisting of: implantation, mucosal, injection, inhalation, and oral.

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60. The method of claim 52, wherein the compound is administered in combination with an additional drug for treating a neurological disorder.

20 61. A composition comprising an antimicrobial compound and a compound for preventing and/or treating a neurological disorder.

62. The composition of claim 61, wherein the antimicrobial compound is selected from the group consisting of cloxyquin, citrinin, iodoquinol, oxyquinoline, and analogs, derivatives, and variants thereof.

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63. The composition of claim 61, wherein the compound for treating a neurological disorder is selected from the group consisting of: nordihydroguaiaretic acid (NDGA), ebselen, flunisolid, hydrocortisone, and analogs, derivatives, and variants thereof.

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64. The composition of claim 61, wherein the neurological disorder is selected from the group consisting of cerebrovascular accident, stroke, seizure, head and spinal cord trauma, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, epilepsy, glaucoma, and hepatic encephalopathy.

65. The composition of claim 61, wherein the compound is linked to a targeting molecule.

66 The composition of claim 65, wherein the targeting molecule's target is a cell selected
5 from the group consisting of glial cells and neuronal cells.

67. The composition of claim 61, wherein the compound is a pro-drug.

68. The composition of claim 61, wherein the compound is formulated for implantation,
10 mucosal, injection, inhalation, or oral administration.